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Safety profile of the varicella vaccine (Oka vaccine strain) based on reported cases from 2005 to 2015 in Japan ☆

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ABSTRACT

Background: As of 2014, routine vaccination strategies in Japan have included the varicella vaccine. Given the widespread use of the vaccine, it is important to investigate the safety profile of the vaccine strain, Oka/Biken varicella, in Japanese patients.
Methods: Reports of adverse events associated with varicella vaccination between 2005 and 2015 were retrospectively reviewed. Virological analysis was performed on clinical specimens collected from some of the reported cases to determine whether the etiological agent was the wild-type or Oka vaccine–strains.
Results: There were 351 reports (3.71/100,000 doses) of adverse events during the observation period. Among the 351 reports, there were 88 reports (0.93/100,000 doses) of varicella-like and 66 reports (0.70/100,000 doses) of zoster-like skin rashes. The wild-type strain induced varicella-like skin rashes earlier than the Oka vaccine strain. The Oka vaccine strain induced zoster-like skin rashes in younger patients compared to the wild-type strain. The onset of zoster-like skin rashes after vaccination was earlier in patients vaccinated with the Oka vaccine–type strain.
Conclusion: The Oka/Biken vaccine is generally safe and well tolerated in Japan. Clinical aspects of adverse reactions caused by the Oka vaccine strain were consistent with previous reports from the United States and Europe.

1. Introduction

The live attenuated varicella vaccine derived from the Oka strain was developed by Takahashi in 1974 [1]. Initially, varicella vaccine was developed for preventing fatal varicella in immunocompromised children such as patients with leukemia [2–4] and nephrotic syndrome [1]. The prophylactic use of the varicella vaccine was approved in Japan in 1986. This vaccine contains a minimum of 1000 plaque-forming units of Oka/Biken varicella virus in 0.5-mL dose when reconstituted by 0.7-mL sterile preparation. Before reconstitution, this vaccine is stored under 5 °C. It has been demonstrated that cold chain of vaccine products was well maintained in Japan. In healthy Japanese children, a single dose of the varicella vaccine induced strong immunity that persisted for 20 years [5]. Previous studies conducted in the United States demonstrated the efficacy of the varicella vaccine following the adoption of the universal immunization against varicella in 1996 [6–10]. Although the varicella vaccine was developed almost four decades ago in Japan, the vaccine has been administered on a voluntary basis until 2014. Therefore, in Japan, vaccine coverage has been insufficient to control the epidemic of varicella as evidenced by a consistent seasonal epidemiological pattern of varicella [11]. In Japan, varicella vaccination has been approved for children over 1 year old and adults without past history of varicella. Varicella vaccine has been generally administered on upper arm in Japan to date. Indeed, recently, as many vaccines have been recommended as routine immunization as similar to United States and European countries, administration of varicella vaccine on leg will be common in future. As co-administration of the vaccine with measles and rubella vaccine has been approved, these two vaccines have been administered simultaneously, indeed precise number of subjects with co-administration of the two vaccine is unclear.

The two commercially available varicella vaccines were derived from the original Biken Oka strain (Oka/Biken): (Oka/Merck: VARIVAX and Oka/RIT: VARILRIX). In postmarketing studies to evaluate the safety profile of these vaccines, both vaccines were safe and

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only induced severe adverse reactions in a rare number of cases [12–16]. Following the adoption of the universal immunization of the Oka/Biken varicella vaccine in Japan, number of children received with varicella vaccine will increase immediately. Therefore, it is important to determine the safety profile of the Oka/Biken varicella vaccine in Japan. In this study, we examined reports of adverse events between 2005 and 2015.

2. Methods

2.1. Postmarketing surveillance

The postmarketing reporting system for adverse reactions is a passive, spontaneous, voluntary reporting system from health care professionals and consumers to Biken. All reported adverse events were collected in a database. In this study, we analyzed all adverse events after varicella vaccination that reported from January 1, 2005 to June 30, 2015. The database contained information about vaccine lot, vaccination date, interval between vaccination and onset of the skin rash, site of skin rash (in cases with herpes zoster), clinical course and outcome, underlying diseases, and demographic information. In vaccine recipients who developed varicella- or zoster-like skin eruptions, physicians ordered virological tests on clinical specimens, such as crusts and vesicular fluid, to differentiate between the wild-type and Oka vaccine strains.

2.2. Case definitions

Varicella vaccine–associated skin rash were categorized as either varicella-like skin rash occurred within 42 days after vaccination or zoster-like skin rash after vaccination. Skin eruptions that were reported as "zoster" or "zoster-like" skin rashes were defined as zoster-like skin rashes.

2.3. Virological analysis

Clinical specimens that were transferred to Biken were subjected to molecular epidemiological analyses. Total DNA was extracted from the specimens using the DNeasy Tissue Kit (QIAGEN, Hilden, Germany). Two methods were performed to differentiate between the Oka vaccine and wild-type strains. (1) Prior to 2006, restriction enzyme fragment length polymorphism (RFLP) analysis of gene 62 was performed. A fragment of gene 62 was amplified by PCR and the PCR product was digested with the restriction enzymes *BssH*II and *Nae*I. The digested products resolved on a 4% agarose gel containing ethidium bromide [17]. (2) After 2006, SNPs analysis of gene 62 using allelic discrimination (AD) real-time PCR was carried out [18]. Real-time PCR was performed with two primer sets for DNA fragments containing SNPs position 107,136 (forward primer, 5′-GTA AAC GAT CAT CCG GTG GAC A-3′; reverse primer, 5′-CGG TCA CCC TTC TCC AAC AAC-3′) and position 107,252 (forward primer, 5′-ACT GGA GCC CGT TGC CTC-3′; reverse primer, 5′-TCC TAC AGA GTC TCC GCA GAG C-3′). Four TaqMan® MGB probes were used for differentiation of the Oka vaccine strain (probe for position 107,136, 5′-VIC-ACA GAA AGA GAG CGC GC-MGB-3′; position 107,252, 5′-VIC-TTG CCG GCA TGG C-MGB-3′) and the wild-type strain (probe for position 107,136, 5′-FAM-CAC AGA AAG AGA GCG TGC-MGB-3′; position 107,252, 5′-FAM-TTG CCA GCA TGG C-MGB-3′). Clinical specimens that tested positive for the Oka vaccine strain using either method (1) or (2) were further subjected to direct sequencing of gene 62 [17].

3. Results

From 2005 to 2015, Biken produced 9.47 million vials of the live attenuated varicella vaccine (Oka/Biken). There were 351 reports (3.71/100,000 doses) of the adverse events during the observation period. Of the 351 reports of adverse events, there were 88 reports (0.93/100,000 doses) of varicella-like skin rashes and 66 reports (0.70/100,000 doses) of zoster-like skin rashes (Table 1). Virological analyses of clinical specimens from 40 of the 88 reports of varicella-like skin rashes detected the Oka vaccine strain in 16 reported cases (0.17/100,000 doses) and the wild-type strain in 15 reported cases (0.16/100,000 doses). Meanwhile, virological analyses of clinical specimens from 48 of the 66 reports of zoster-like skin rash detected the Oka vaccine strain in 10 reported cases (0.11/100,000 doses) and the wild-type strain in 25 reported cases (0.26/100,000 doses).

3.1. Varicella-like skin rash within 42 days after vaccination

Clinical characteristics were compared between the cases with varicella-like skin rash caused by the Oka vaccine strain (n = 16) and those caused by the wild-type strain (n = 15) (Table 2). The wild-type strain induced a skin rash by a median of 12 days (range 0–16 days) after vaccination, which was shorter than that of the Oka vaccine strain (median of 25 days, range 14–42 days). The frequency of underlying diseases in the vaccine recipients was higher in patients of the Oka vaccine strain (13 of the 16 cases had underlying diseases) compared to patients of the wild-type strain (2 of the 15 cases had underlying diseases).

Clinical information for the six severe cases caused by the Oka vaccine strain is summarized in Table 3. Four of the six cases were clearly immunocompromised, including kidney transplant recipients and patients treated with immunosuppressive drugs. One of the four patients who recovered, severe neurological impairments were detected. Two of the six cases were fatal (Table 4); one of the two cases was kidney transplant recipient treated with several immunosuppressive drugs, and another case had severe neurological impairments without immunosuppressive treatment. These two fatal cases were confirmed as severe VZV infection caused

Table 1
Incidence of varicella-like skin rash and zoster-like skin rash after vaccination.

	Number of reports	Incidence[b] (/100,000 doses)
All reported adverse events	351	3.71
-Cannot rule out the relationship with immunization	252	2.66
Skin eruptions[a]	244	2.58
Skin eruptions (except varicella-like and herpes zoster like eruptions)	69	0.73
-Cannot rule out the relationship with immunization	60	0.63
Varicella-like	109	1.15
Occurred within 42 days	88	0.93
Vaccine strain	16	0.17
Wild type strain	15	0.16
VZV-negative	9	0.10
Not analyzed	48	0.51
Herpes zoster-like	66	0.70
Vaccine strain	10	0.11
Wild type strain	25	0.26
VZV-negative	13	0.14
Not analyzed	18	0.19

[a] "Skin eruptions" include varicella-like and herpes zoster-like skin eruptions, asthma, hives, erythema multiforme, redness and so on (except injection site reaction).
[b] Incidence was calculated events number against vaccine products, 9,467,000.

Table 2
Comparison of clinical characteristics between the patients with varicella-like skin rash within 42 days after vaccination caused by Oka-vaccine strain and those caused by wild-type.

Variable	Vaccine type	Wild type
Numbers of reports	16	15
Age (median; range)	3 (1–40)	1.5 (1–48)
Gender (female/male)	1 (8/8)	0.875 (7/8)
Days between onset of skin rash and vaccination (median; range)	25 (14–42)	12 (0–16)
Severity (non-severe/severe)	10/6	13/2
Outcome (recover/sequelae/fatal/unknown)	13/0/2/1	12/0/0/3
Underlying diseases (yes/no)	13/3	2/13

by Oka-vaccine strain based on molecular epidemiological analysis. Although the patients were received intensive treatments including acyclovir administration soon after the onset of the diseases, the treatments were unsuccessful.

3.2. Zoster-like skin rash

Clinical characteristics were compared between the cases with zoster-like skin rashes caused by the Oka vaccine strain (n = 10) and those caused by the wild-type strain (n = 25) (Table 5). The median age of the cases with the Oka vaccine–type strain (median age of 1 year old) was lower than the wild-type strain (median age of 9.5). The onset of zoster-like skin rashes after vaccination was earlier in cases with the Oka vaccine–type strain (median of 167 days) compared to cases with the wild-type strain (median of 2506 days). Although half of the cases with Oka vaccine strain–related zoster-like skin rashes were defined as severe cases, all of these cases were completely recovered. In cases of either the Oka vaccine–type or wild-type strains, some of the zoster-like skin rashes were associated with underlying diseases.

As shown in Table 6, various dermatomes were involved in the patients regardless to the causative strains. Although Oka vaccine strain DNA was detected in the five skin rashes located in the vaccination sites, no wild-type strain DNA was detected in the clinical samples collected from the dermatome.

4. Discussion

Postmarketing surveillance is conducted to analyze large numbers of vaccine recipients for the detection of rare adverse reaction. However, a major limitation of postmarketing surveillance is the reliance on voluntary reporting by healthcare professionals and consumers. In some instances, adverse events may be underreported or go unreported all together. Since the introduction of universal immunization against varicella using the Oka/Merck vaccine in the United States and Europe, several postmarketing surveillances in these countries have been conducted [12,15]. The Oka/Merck varicella vaccine was generally well tolerated and the most frequent adverse reaction was skin rashes. Despite the development of the Oka vaccine strain by Takahashi in Japan in 1974 [1], to date there have been no reports of postmarketing surveillance data because the varicella vaccine was a voluntary vaccination until 2014. Although breakthrough varicella could be analyzed using the same database used in this current study, analysis of breakthrough varicella is difficult because the numbers of breakthrough varicella cases remain high in Japan. Therefore, in this study, we analyzed reports of varicella-like skin rashes within 42 days after vaccination and zoster-like skin rashes.

The incidence of reported adverse events in this study is approximately one-tenth of those in the previous postmarketing reports of the Oka/Merck vaccine [12,15]. Although the precise explanation for this low incidence of adverse events in our study is difficult to assert, some key differences may include our reporting system or the racial make-up of the patients.

Previous postmarketing surveillance data revealed that varicella-like skin rashes within 2 weeks after vaccination were more commonly associated with the wild-type strain [12]. The present data also demonstrated that the interval between vaccination and the appearance of the skin rash was shorter in patients with the wild-type strain (median of 12 days) than those with the Oka vaccine strain (median of 25 days). It is noteworthy that the wild-type strain was rarely detected beyond two weeks after vaccination. Moreover, the rate of underlying diseases was higher in cases of skin rashes caused by the Oka vaccine strain than those caused by the wild-type strain, suggesting that patients with underlying disease may be at high risk for skin rashes caused by varicella vaccine. Of the six severe cases, including two fatal cases, varicella-like skin rashes were caused by the Oka vaccine strain (Tables 3 and 4). Similar to previous studies [12,15], most of the patients were immunocompromised. Based on the clinical research that evaluated the safety and efficacy of the Oka/Biken varicella vaccine, the criteria for administration of the vaccine in acute lymphoblastic leukemia and nephrotic syndrome treated with steroid were defined [2]. Several severe adverse reactions, including fatal outcomes, have been demonstrated in acquired [19,20] and congenital immunosuppressed patients [21–24]. Similar findings were reported in this current study suggesting that the varicella vaccine should be carefully administered to immunocompromised patients, as well as patients with severe neurological deficit including cerebral paralysis may be high risk for varicella vaccine. Although similar cases were previously reported based on post licensure safety surveillance in the United States [14], further detailed analysis is required to determine whether those patients are high risk. In the congenital immunodeficiency patients, it was difficult to predict most of the severe or fatal varicella cases due to the Oka vaccine strain before vaccination [21–24]. Thus, healthcare professionals should carefully review patient medical records to identify potential factors that may lead to complications. Although varicella vaccine was initially developed for protection of immunocompromised children [2–4], effective antiviral drugs

Table 3
Summary of severe cases of Oka vaccine-strain associated varicella-like skin rash occurred within 42 days after vaccination.

Case No.	Vaccination year	Onset (day)	Outcome	Immunocompromised	Underlying diseases
1	2012	12[a]	Fatal	Yes	Kidney transplant
2	2013	42	Recovered	Yes	Kidney transplant
3	2013	25	Recovered	Possible	Hypoxic encephalopathy
4	2013	23	Recovered	Yes	Nephrotic syndrome
5	2014	25	Fatal	Possible	Cerebral palsy
6	2015	20	Recovered	Yes	Hepatoblastoma

[a] 12 days after from secondary vaccination, which mean 45 days after from first vaccination. All other cases received 1 dose of varicella vaccine.

Table 4
Summary of the two fatal cases after varicella vaccination.

Case	Age (yrs)	Gender	Underlying condition or disease	Immunosuppressive drugs	Interval between vaccination and disease onset/ and death (days)	Cause of death
1	40	Male	Renal transplantation due to chronic RF	MMF, CyA, mPSL	45 (after 1st shot)/173 (after 1st shot) 12 (after 2nd shot)	Disseminated varicella[a] DIC
2	2	Female	CP due to neonatal asphyxia receiving mechanical ventilation	N/A	25/36	Varicella[a] DIC SIRS

RF; renal failure, DIC; disseminated intravascular coagulopathy, CP; cerebral paralysis, SIRS; systemic inflammatory response syndrome, MMF; Mycophenolate mofetil, CyA; cyclosporine, mPSL; methyl prednisolone.
[a] Both cases were confirmed with Oka-vaccine strain infection by using SNPs analysis and direct sequencing of gene 62.

Table 5
Comparison of clinical characteristics between the patients with zoster-like skin rash caused by Oka-vaccine strain and those caused by wild-type strain.

Variable	Vaccine type	Wild type
Numbers of reports	10	25
Age (median; range)	1 (1–4)	9.5 (1–72)
Gender (female/male)	1.0 (5/5)	1.8 (16/9)
Days between onset of skin rash and vaccination (median; range)	167 (11–855)	2506 (10–5110)
Severity (non-severe/severe)	5/5	12/13
Outcome (recover/sequelae/fatal/ unknown)	9/0/0/1	21/0/0/4
Underlying diseases (yes/no)	3/7	4/21

Table 6
Regions of zoster-like skin rash; comparison between Oka-vaccine strain and wild type strain.

Regions	Vaccine type (10 cases)	Wild type (25 cases)
Site of the vaccination (upper arm)	5	0
Face	1	6
Ear	0	4
Ocular	0	1
Neck	2	4
Anterior chest	2	2
Back	5	2
Abdomen	1	2
Lumber	1	2
Buttock	1	2
Genital	1	1
Lower extremity	0	0

are currently available to treat the patients. Physician has to administer the vaccine carefully to immunocompromised host to avoid severe adverse reaction.

This study demonstrated that zoster-like skin rashes caused by the Oka vaccine strain occurred in younger individuals compared to skin rashes caused by the wild-type strain. The interval between vaccination and the onset of zoster-like skin rashes was shorter in the cases caused by the Oka vaccine strain than those caused by the wild-type strain. These two findings are consistent with previous postmarketing studies [12,15]. In the previous postmarketing surveillances in the United States and Europe [12,15,16], the vaccine strain was frequently detected in patients with zoster-like skin rashes after vaccination. In contrast to those studies, our study detected more cases with zoster-like skin rashes with the wild-type strain than the Oka vaccine strain. The differences between our data and previous reports may be related to differences between the surveillance systems as well as distinct properties of the prevalence of varicella virus in the United States and Europe compared to Japan. Taken together, these data indicate that the Oka vaccine strain can be reactivated even in immunocompetent hosts resulting in zoster. In recent studies, however, the incidence of zoster was significantly lower in vaccine recipients than patients with natural varicella [25–27]. Therefore, universal immunization with the varicella vaccine is an appropriate strategy for controlling both varicella and zoster.

As similar to previous studies [12,15], all of zoster-like skin rashes at the administration site were caused by the Oka vaccine strain. However, it is difficult to identify the causative strain based on the clinical symptoms of the zoster-like skin rash because the Oka vaccine strain was detected in the various dermatomes of the zoster-like skin rashes. It has been demonstrated that the reactivation of the wild-type strain can cause a severe form of zoster in vaccine recipients without a history of natural varicella [28], which may be caused by subclinical wild-type varicella infection suggested by Hammershiag et al. [29]. Therefore, if a physician observes zoster-like skin rashes in vaccine recipients, they should distinguish between the Oka vaccine type and wild-type strains to evaluate vaccine safety. Laboratory testing system for differentiation between Oka vaccine strain and wild-type strain has been managed by Merck and Columbia University in New York. In Japan, it is necessary to develop similar molecular epidemiological monitoring system to evaluate vaccine safety in future.

References

[1] Takahashi M, Otsuka T, Okuno Y, Asano Y, Yazaki T. Live vaccine used to prevent the spread of varicella in children in hospital. Lancet 1974;2(7892):1288–90.
[2] Hattori A, Ihara T, Iwasa T, Kamiya H, Sakurai M, Izawa T, et al. Use of live varicella vaccine in children with acute leukaemia or other malignancies. Lancet 1976;2(7978):210.
[3] Izawa T, Ihara T, Hattori A, Iwasa T, Kamiya H, Sakurai M, et al. Application of a live varicella vaccine in children with acute leukemia or other malignant diseases. Pediatrics 1977;60(6):805–9.
[4] Ha K, Baba K, Ikeda T, Nishida M, Yabuuchi H, Takahashi M. Application of live varicella vaccine to children with acute leukemia or other malignancies without suspension of anticancer therapy. Pediatrics 1980;65(2):346–50.
[5] Asano Y, Suga S, Yoshikawa T, Kobayashi I, Yazaki T, Shibata M, et al. Experience and reason: twenty-year follow-up of protective immunity of the Oka strain live varicella vaccine. Pediatrics 1994;94(4 Pt 1):524–6.
[6] Patel RA, Binns HJ, Shulman ST. Reduction in pediatric hospitalizations for varicella-related invasive group A streptococcal infections in the varicella vaccine era. J Pediatr 2004;144(1):68–74.
[7] Guris D, Jumaan AO, Mascola L, Watson BM, Zhang JX, Chaves SS, et al. Changing varicella epidemiology in active surveillance sites–United States, 1995–2005. J Infect Dis 2008;197(Suppl 2):S71–5.
[8] Davis MM, Patel MS, Gebremariam A. Decline in varicella-related hospitalizations and expenditures for children and adults after introduction of varicella vaccine in the United States. Pediatrics 2004;114(3):786–92.
[9] Nguyen HQ, Jumaan AO, Seward JF. Decline in mortality due to varicella after implementation of varicella vaccination in the United States. N Engl J Med 2005;352(5):450–8.
[10] Seward JF, Watson BM, Peterson CL, Mascola L, Pelosi JW, Zhang JX, et al. Varicella disease after introduction of varicella vaccine in the United States, 1995–2000. JAMA 2002;287(5):606–11.
[11] Ozaki T. Varicella vaccination in Japan: necessity of implementing a routine vaccination program. J Infect Chemother 2013;19(2):188–95.

[12] Galea SA, Sweet A, Beninger P, Steinberg SP, Larussa PS, Gershon AA, et al. The safety profile of varicella vaccine: a 10-year review. J Infect Dis 2008;197 (Suppl 2):S165–9.
[13] Sharrar RG, LaRussa P, Galea SA, Steinberg SP, Sweet AR, Keatley RM, et al. The postmarketing safety profile of varicella vaccine. Vaccine 2000;19(7–8):916–23.
[14] Wise RP, Salive ME, Braun MM, Mootrey GT, Seward JF, Rider LG, et al. Postlicensure safety surveillance for varicella vaccine. JAMA 2000;284 (10):1271–9.
[15] Goulleret N, Mauvisseau E, Essevaz-Roulet M, Quinlivan M, Breuer J. Safety profile of live varicella virus vaccine (Oka/Merck): five-year results of the European Varicella Zoster Virus Identification Program (EU VZVIP). Vaccine 2010;28(36):5878–82.
[16] Chaves SS, Haber P, Walton K, Wise RP, Izurieta HS, Schmid DS, et al. Safety of varicella vaccine after licensure in the United States: experience from reports to the vaccine adverse event reporting system, 1995–2005. J Infect Dis 2008;197(Suppl 2):S170–7.
[17] Gomi Y, Imagawa T, Takahashi M, Yamanishi K. Oka varicella vaccine is distinguishable from its parental virus in DNA sequence of open reading frame 62 and its transactivation activity. J Med Virol 2000;61(4):497–503.
[18] Campsall PA, Au NH, Prendiville JS, Speert DP, Tan R, Thomas EE. Detection and genotyping of varicella-zoster virus by TaqMan allelic discrimination real-time PCR. J Clin Microbiol 2004;42(4):1409–13.
[19] Kramer JM, LaRussa P, Tsai WC, Carney P, Leber SM, Gahagan S, et al. Disseminated vaccine strain varicella as the acquired immunodeficiency syndrome-defining illness in a previously undiagnosed child. Pediatrics 2001;108(2):E39.
[20] Schrauder A, Henke-Gendo C, Seidemann K, Sasse M, Cario G, Moericke A, et al. Varicella vaccination in a child with acute lymphoblastic leukaemia. Lancet 2007;369(9568):1232.
[21] Levy O, Orange JS, Hibberd P, Steinberg S, LaRussa P, Weinberg A, et al. Disseminated varicella infection due to the vaccine strain of varicella-zoster virus, in a patient with a novel deficiency in natural killer T cells. J Infect Dis 2003;188(7):948–53.
[22] Jean-Philippe P, Freedman A, Chang MW, Steinberg SP, Gershon AA, LaRussa PS, et al. Severe varicella caused by varicella-vaccine strain in a child with significant T-cell dysfunction. Pediatrics 2007;120(5):e1345–9.
[23] Levin MJ, Dahl KM, Weinberg A, Giller R, Patel A, Krause PR. Development of resistance to acyclovir during chronic infection with the Oka vaccine strain of varicella-zoster virus, in an immunosuppressed child. J Infect Dis 2003;188 (7):954–9.
[24] Banovic T, Yanilla M, Simmons R, Robertson I, Schroder WA, Raffelt NC, et al. Disseminated varicella infection caused by varicella vaccine strain in a child with low invariant natural killer T cells and diminished CD1d expression. J Infect Dis 2011;204(12):1893–901.
[25] Hardy I, Gershon AA, Steinberg SP, LaRussa P, Varicella Vaccine Collaborative Study Group. The incidence of zoster after immunization with live attenuated varicella vaccine. A study in children with leukemia. N Engl J Med 1991;325 (22):1545–50.
[26] Takahashi M, Baba K, Horiuchi K, Kamiya H, Asano Y. A live varicella vaccine. Adv Exp Med Biol 1990;278:49–58.
[27] Schmid DS, Jumaan AO. Impact of varicella vaccine on varicella-zoster virus dynamics. Clin Microbiol Rev 2010;23(1):202–17.
[28] Ibraheem M, Marin M, Leung J, Bryce CH, Schmid DS, Zaki SR, et al. Fatal wild-type varicella-zoster virus encephalitis without a rash in a vaccinated child. Pediatr Infect Dis J 2013;32(2):183–5.
[29] Hammerschlag MR, Gershon AA, Steinberg SP, Clarke L, Gelb LD. Herpes zoster in an adult recipient of live attenuated varicella vaccine. J Infect Dis 1989;160 (3):535–7.